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Silylation of Alcohols and Phenols with Hexamethyldisilazane over Highly Reusable Propyl Sulfonic Acid Functionalized Nanostructured SBA-15

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Abstract: Various alcohols and phenols were trimethylsilylated in excellent yields using hexamethyldisilazane in the presence of catalytic amounts of environmentally friendly, hydrophobic, highly thermal stable, and completely heterogeneous sulfonic acid functionalized mesostructured SBA-15 in dichloromethane at ambient temperature. Primary, bulky secondary, tertiary, and phenolic hydroxyl functional groups were transformed to the corresponding trimethylsilyl ethers in excellent yields. The simple experimental procedure was accompanied by easy recovery and the catalyst was reusable (at least 18 reaction cycles); these are attractive features of this protocol.

Key words: reusable heterogeneous catalyst; solid sulfonic acid; SBA-15; protecting group; silylation; hexamethyldisilazane

The protection of the hydroxyl function in alcohols and phenols is a common and versatile part of many syntheses of reasonable complexity. Among the routinely employed methodologies for the masking of hydroxyl groups in organic chemistry, the transformation of alcohols to the corresponding silyl ethers is a popular procedure [1,2]. The popularity and extensive use of silyl ethers as protecting groups for alcohols come from their ease of formation, resistance to oxidation, good stability toward most non-acidic reagents, and easy deprotection to provide free alcohols [3]. Although many reagents are available for the silylation of hydroxyl groups [4–13], some of these methods suffered from serious drawbacks such as the lack of reactivity, low product yields, long reaction times, expensive reagents and catalysts, and robust purification steps or difficulty in by-product removal. In contrast, 1,1,1,3,3,3-hexamethyldisilazane (HMDS) is a cheap, easy handling, commercially available and stable reagent, and it is frequently used for the trimethylsilylation of hydroxyl groups giving ammonia as the only by-product. However, the main drawback of HMDS is its poor silylating power as it needs forceful conditions and long reaction times in many instances [14]. Therefore, a variety of catalysts have been developed for the activation of this reagent such as sulfuric acid [2], $(CH_3)_3SiCl$ [15], sulfonic acids [16], K-10 montmorillonite [17,18], iodine [19], tungstophosphoric acid ($H_3PW_{12}O_{40}$) [20], $LiClO_4$ [21], TBBDA and PBBS [22], $[PdCl(\eta^3\text{-}C_3H_5)]_2\text{-}PPh_3$ [23], $HReO_4$ [24], $LaCl_3$ [25], tribromomelamine [26], $Bi(OTf)_3$ [27], tribromoisocyanuric acid and DABCO-Br [28]. Although the silylation ability of HMDS has been improved by these methods, some problems such as the use of a corrosive catalyst, drastic reaction conditions, tedious workup, and long reaction times still need to be overcome. Moreover, many of these reagents are expensive and non-recoverable leading to the generation of a large amount of toxic waste particularly when large-scale applications are considered. In other words, the tightening of legislation with regard to the treatment and disposal of toxic waste produced during the difficult separation of the desired products is forcing industry to consider greener technologies. Therefore, solid acids catalysis is a growing field of research as the demand for clean and eco-friendly chemical processes is increasing [29–34]. Accordingly, chemical industry is currently searching for highly active, stable, and recyclable solid acids to improve the environmental safety of the production of chemicals under milder reaction conditions. To address these issues, Zareyee and Karimi [35] demonstrated the application of recoverable sulfonic acid functionalized ordered mesoporous silica (MCM-41-Pr-SO₃H) for the efficient silylation of alcohols and phenols. Quite recently, they

used a heterogeneous and hydrophobic sulfonic acid nanoreactor with acidic sites and phenyl groups within the mesochannel of SBA-15 as an efficient, environmentally benign, and highly recoverable catalyst for the Pechmann [36] and Strecker [37] reactions. In the course of our ongoing green organic chemistry program and current interest in the development of nanostructured solid acids for different organic transformations [35–39], we report on a brief preparation and application of a sulfonic acid nanoreactor (SBA-15-Ph-Pr-SO$_3$H) for the trimethylsilylation of hydroxyl groups.

1 Experimental

1.1 Preparation of SBA-15-Ph-Pr-SO$_3$H

The synthesis of SBA-15-Pr-SH was achieved using the known procedure described by Stucky et al. [40]. This procedure involved a synthetic strategy based on the co-con- densation of tetraethoxysilane (TEOS) and 3-mercaptopro- pyltrimethoxysilane (MPTMS) in the presence of Pluronic P123 as the structure directing agent. In a typical preparation procedure, 4 g of Pluronic P123 (Aldrich, average $M_w = 5800$) was dissolved in 125 g of 1.9 mol/L HCl solution with stirring at room temperature. The solution was heated to 40 °C before adding 6.83 g TEOS. After a 3 h pre-hydrolysis of TEOS, 1.6 g thiol precursor MPTMS was added. The resultant solution was stirred for 20 h at 40 °C after which the mixture was aged at 100 °C for 24 h under static conditions. The solid was recovered by filtration and air dried at room temperature overnight. The template was removed from the as-synthesized material by washing with ethanol using a Soxhlet apparatus for 24 h.

To a suspension of SBA-15-Pr-SH (3 g) in dry toluene PhSi(OEt)$_3$ (PTES, 4 mmol) was added. The resulting mixture was first stirred at room temperature for 1 h and then refluxed for a further 24 h. The solid material was filtered and successively washed with toluene, EtOH, and Et$_2$O and dried overnight at 120 °C to afford the corresponding SBA-15-Ph-Pr-SH.

Conversion of the catalyst's thiol groups to sulfonic acid moieties was accomplished by hydrogen peroxide. Typically, 0.3 g of solid hydrophobic material was suspended in 10 g of aqueous 30 wt% H$_2$O$_2$. This suspension was stirred at room temperature in an Ar atmosphere for 24 h. After the oxidation treatment, the resulting solution was filtered and washed separately with water and ethanol. Finally the wet material was suspended in 1 mol/L H$_2$SO$_4$ solution for 2 h and it was then washed several times with water and ethanol and dried at 60 °C under vacuum overnight to give the corresponding SBA-15-Ph-Pr-SO$_3$H, denoted as catalyst **1** (Fig. 1).

The concentration of sulfonic acid groups in catalyst **1** was quantitatively estimated by ion-exchange pH analysis. To an aqueous solution of NaCl (1 mol/L, 25 ml) with a primary pH of 5.1 the catalyst **1** (100 mg) was added and the resulting mixture was stirred for 6 h after which the pH of the solution
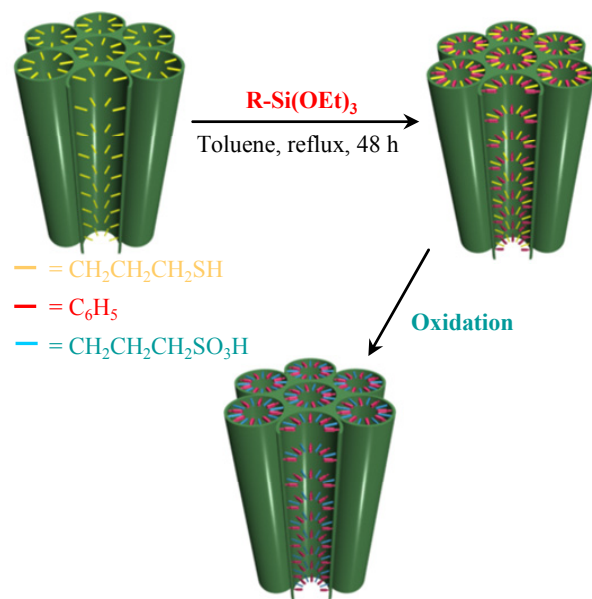

Fig. 1. Schematic representation of the preparation of the sulfonic acid based catalyst **1**.

decreased to 2.19

1.2 General procedure for the trimethylsilylation of alcohols

To a solution of alcohol (1 mmol) and HMDS (0.6 mmol) in dichloromethane (3 ml) catalyst **1** (19 mg, 3 mol%) was added. The mixture was stirred at 35 °C for a period of time (Fig. 2). Reaction progress was monitored by thin layer chromatography (TLC) and gas chromatography (GC). After the completion of the reaction the product was isolated by filtration. Evaporation of the solvent under reduced pressure gave the
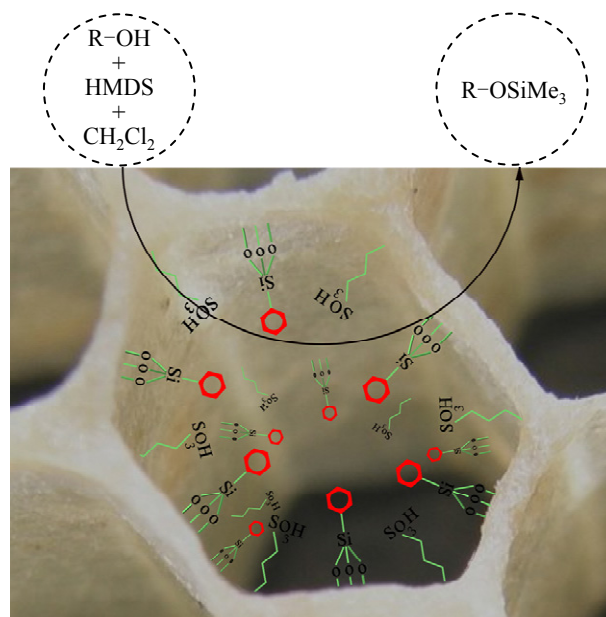
Fig. 2. Silylation reaction using catalyst **1**.

corresponding silyl ether.

2 Results and discussion

2.1 Acid amount of SBA-15-Ph-Pr-SO₃H

The amount of acid in SBA-15-Ph-Pr-SO$_3$H was determined to be 1.61 mmol/g. CHN and thermal gravimetry (TG) analysis (Fig. 3) of the catalyst confirms an acid content of 1.61 mmol/g.

2.2 Trimethylsilylation of alcohols and phenols

As a preliminary study, the catalytic evaluation of SBA-15-Ph-Pr-SO$_3$H towards the synthesis of silyl ether from benzyl alcohol was undertaken.

In an initial attempt, a blank reaction was carried out using 1 equiv. each of benzyl alcohol and HMDS in the presence of 1 mol% (6.3 mg) of SBA-15-Ph-Pr-SO$_3$H. These were stirred at room temperature in CH$_2$Cl$_2$ and the corresponding benzyloxytrimethyl silane was obtained in 50% GC yield after stirring the reaction mixture for 180 min. Increasing the reaction temperature to 35 °C improved the yield of the related product to 80% under the same reaction conditions. Subsequently, to establish the best reaction conditions the same reaction between benzyl alcohol and HMDS in CH$_2$Cl$_2$ at 35 °C was used as a model reaction to screen the effect of catalytic amounts of SBA-15-Ph-Pr-SO$_3$H. The results showed that no appreciable reaction occurred when benzyl alcohol and HMDS were allowed to react in dichloromethane in the absence of a catalyst and the reaction yield was only 20% of expected product after 2 h without a catalyst. This indicates that the catalyst is required for this reaction. Interestingly, 3 mol% of catalyst **1** and 0.6 mmol of HMDS was sufficient to drive the silylation of benzyl alcohol completely over a short reaction time (100% GC yield after 20 min.). Based on these findings and to ascertain the scope and generality of this protocol we screened a range of alcohols and phenols under optimized reaction conditions. As shown in Table 1, a wide range of alcohols underwent silylation by this procedure to provide trimethylsilyl ether in excellent
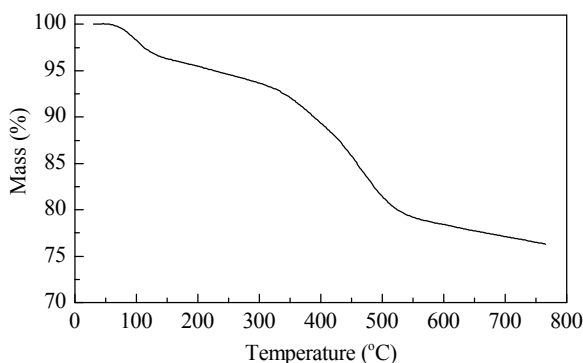

Fig. 3. TG diagram for SBA-15-Ph-Pr-SO$_3$H.

Table 1 Trimethylsilylation of alcohols and phenols using SBA-15-Ph-Pr-SO$_3$H in dichloromethane at 35 °C

Entry	Substrate	Product	Time (min)	Yield[*] (%)
1	benzyl alcohol (OH)	benzyl OTMS	20	100
2	3-Cl-benzyl alcohol	3-Cl-benzyl OTMS	30	97
3	4-Cl-benzyl alcohol	4-Cl-benzyl OTMS	40	96
4	3,5-diCl-benzyl alcohol	3,5-diCl-benzyl OTMS	50	99
5	4-CH$_3$-benzyl alcohol	4-CH$_3$-benzyl OTMS	50	93
6	4-O$_2$N-benzyl alcohol	4-O$_2$N-benzyl OTMS	150	80
7	phenethyl alcohol	phenethyl OTMS	90	99
8	pyrenyl-CH$_2$OH	pyrenyl-CH$_2$OTMS	120	91
9	furfuryl alcohol	furfuryl OTMS	120	89
10	hexanol	hexyl OTMS	150	90
11	octanol	octyl OTMS	150	96
12	2-heptanol	2-heptyl OTMS	180	95
13	2-adamantanol	2-adamantyl OTMS	180	89
14	menthol type OH	OTMS	120	90
15	cyclohexanol	cyclohexyl OTMS	135	91
16	4-t-Bu-cyclohexanol	4-t-Bu-cyclohexyl OTMS	135	93
17	diphenylmethanol	diphenylmethyl OTMS	110	95
18	phenol	phenyl OTMS	120	94
19	4-Cl-phenol	4-Cl-phenyl OTMS	160	92
20	3-NO$_2$-phenol	3-NO$_2$-phenyl OTMS	300	70
21	3,5-diCH$_3$-phenol	3,5-diCH$_3$-phenyl OTMS	150	80
22	1-adamantanol	1-adamantyl OTMS	200	90
23	(Ph)$_3$COH	(Ph)$_3$COTMS	1440	40

[*]GC yield.

Table 2 Comparison of the catalytic efficiency of SBA-15-Ph-Pr-SO₃H with other reported catalysts for the trimethylsilylation of benzyl alcohol using HMDS

Entry	Catalyst (amount)	Solvent	Temperature (°C)	Time (min)	Yield (%)	Ref.
1	SBA-15-Ph-Pr-SO₃H (3 mol%)	CH₂Cl₂	35	20	100	this work
2	H₃PW₁₂O₄₀ (1 mol%)	solvent free	55–60	23	100	[18][a]
3	LiClO₄ (50 mol%)	solvent free	rt	25	99	[19][a]
4	LaCl₃ (10 mol%)	CH₂Cl₂	rt	180	91	[23][a,b]
5	HY Zeolite (0.1 g)	solvent free	55–60	120	80	[18][a,b]
6	Bi(OTf)₃ (5 mol%)	solvent free	rt	4	99	[25][a,b,c]
7	DABCO-Br (0.1 mol%)	CH₃CN	rt	10	100	[28][a,d]

[a]No recovery. [b]Long reaction time. [c]1 mmol HMDS was used. [d]0.8 mmol HMDS was used.

yields. Benzylic, primary, hindered and unhindered secondary, and unhindered tertiary alcohols were silylated in dichloromethane at 35 °C and the reactions were completed over periods ranging from 20 to 1440 min to provide good to excellent yields of the silylated products (Table 1). In the case of primary benzylic and aliphatic alcohols the reactions were complete within 150 min in CH₂Cl₂ at 35 °C accompanied by a fast evolution of NH₃ gas from the reaction mixture (Table 1, entries 1–11). Various benzyl alcohols with electron-donating and electron-withdrawing substituents underwent smooth silylation with excellent yields (Table 1, entries 1–6). The catalytic system is applicable to heterocyclic alcohols such as furfuryl alcohol (Table 1, entry 9). The reaction of primary aliphatic alcohols proceeded in short reaction time with excellent yields (Table 1, entries 10 and 11).

From Table 1, this method is also shown to be efficient for the silylation of secondary aliphatic (Table 1, entries 12–16) and aromatic (Table 1, entry 17) alcohols. Phenol and its derivatives were also silylated in an efficient manner in excellent yields (Table 1, entries 18–21). These encouraging results prompted us to test the trimethylsilylation of hindered tertiary alcohols. Even though 1-adamantanol was converted to the corresponding silylated product in good yield (Table 1, entry 22), for the less reactive triphenylmethanol longer reaction time was necessary to afford the desired product. However, triphenylmethanol gave the related trimethylsilyl ether in 40% yield after 24 h (Table 1, entry 23). For the hindered secondary and tertiary alcohols no elimination of by-products were observed.

After achieving this favorable result, we compared the results of the silylation of alcohols with our previously reported catalyst (MCM-41-Pr-SO₃H) to determine the effectiveness of this catalyst. Our evaluation showed that the higher conversion of starting materials for catalyst **1** in comparison to MCM-41-Pr-SO₃H was likely due to the larger pore size of SBA-15 and the beneficial influence of phenyl groups in close proximity to the sulfonic acid groups. Based on these observations it is clear that the pore size and the hydrophobic character of catalyst **1** is crucial for the effectiveness of this sulfonic acid based catalyst for the catalysis of the silylation reaction.

Recycling of the catalyst was explored upon the silylation of benzyl alcohol with HMDS. After the completion of the first run, which affords the corresponding benzyloxytrimethyl silane in 100% yield, the products and the solvent were removed from the reaction mixture using a syringe, and fresh reactants and solvent were added to the catalyst to run the second silylation reaction. Gratifyingly, SBA-15-Ph-Pr-SO₃H was successfully reused in eighteen successive runs and exhibited consistent activity to afford an average yield of 99.5% with virtually no significant loss of performance, which clearly demonstrates the practical recyclability of this catalyst. This reusability demonstrates the high stability and turnover of the catalyst under the conditions employed.

To compare the catalytic potential of catalyst **1** with some recently reported catalysts, we studied the silylation of benzyl alcohol using HMDS in the presence of various catalysts (Table 2). The results show that some protocols took longer, some used dangerous materials with reduced isolated yields and some used non-recoverable catalysts, which clearly shows that SBA-15-Ph-PrSO₃H should be considered one of the best choices.

3 Conclusions

SBA-15-Ph-Pr-SO₃H was a highly efficient and recoverable catalyst for the silylation of alcohols and phenols by HMDS in dichloromethane at 35 °C. The most striking features of this method are excellent catalytic capacity, outstanding stability, exceedingly simple workup, and multiple reuse of SBA-15-Ph-Pr-SO₃H. As a consequence, this system represents a substantial improvement over previous methods wherein product separation produces a large amount of waste. In addition, by this method, primary, bulky secondary, tertiary, and phenolic hydroxyl functional groups are protected with excellent yields. Further studies will focus on the exploration of this solid sulfonic acid for other types of functional group transformations.

Acknowledgments

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